

L6 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:654747 CAPLUS

DOCUMENT NUMBER: 135:222364

TITLE: DNA sequence of human prostaglandin E2 receptor 1 (**EP1-R**) gene, and methods for the diagnosis of **polymorphisms** thereof

INVENTOR(S): Smith, John Craig; Anand, Rakesh; Morten, John Edward Norris

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1130122	A2	20010905	EP 2001-301291	20010213
EP 1130122	A3	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002076702	A1	20020620	US 2001-781311	20010213
JP 2001286288	A2	20011016	JP 2001-40076	20010216
PRIORITY APPLN. INFO.:			GB 2000-3553	A 20000217
			GB 2000-8376	A 20000406

AB The invention provides the genomic DNA sequence of the human prostaglandin

E2 receptor 1 (EP1-R) gene; it differs from the cDNA sequence of EMBL L22647 and the DNA sequence of EMBL AC008569. The invention also provides

methods of diagnosing fourteen specific **polymorphisms** in the **EP1-R** gene and novel allelic polypeptides encoded thereby. The invention provides allele-specific probes and/or primers for

use in diagnosis. The invention also relates to methods of diagnosis and treatment of EP1-R ligand mediated diseases, such as cancer or arthritis.

L10 ANSWER 16 OF 17

MEDLINE

DUPLICATE 6

ACCESSION NUMBER: 2000005672 MEDLINE  
DOCUMENT NUMBER: 20005672 PubMed ID: 10537280  
TITLE: Role of the **prostaglandin E receptor**  
subtype **EP1** in colon carcinogenesis.  
AUTHOR: Watanabe K; Kawamori T; Nakatsugi S; Ohta T; Ohuchida S;  
Yamamoto H; Maruyama T; Kondo K; Ushikubi F; Narumiya S;  
Sugimura T; Wakabayashi K  
CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center  
Research  
Institute, Tokyo, Japan.  
SOURCE: CANCER RESEARCH, (1999 Oct 15) 59 (20) 5093-6.  
Journal code: 2984705R. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199911  
ENTRY DATE: Entered STN: 20000111  
Last Updated on STN: 20000111  
Entered Medline: 19991110

AB Although the cyclooxygenase pathway of the arachidonic acid cascade has been suggested to play an important role in colon carcinogenesis, the molecular species of prostanoids and receptors involved have not been fully elucidated yet. We examined the development of aberrant crypt foci (ACFs), putative preneoplastic lesions of the colon, in two lines of knockout mice, each deficient in **prostaglandin E receptors, EP1** and EP3, by treatment with the colon carcinogen, azoxymethane. Formation of ACFs was decreased only in the EP1-knockout mice to approximately 60% of the level in wild-type mice. Administration of 250, 500, or 1000 ppm of a novel selective EP1 antagonist, ONO-8711, in the diet to azoxymethane-treated C57BL/6J mice also resulted in a dose-dependent reduction of ACF formation. Moreover, when Min mice, having a nonsense mutation in the adenomatous polyposis coli gene, were given 500 ppm ONO-8711 in the diet, the number of intestinal polyps was significantly reduced to 57% of that in the basal diet group. These results strongly suggest that prostaglandin E2 contributes to colon carcinogenesis to some extent through its action at the EP1 receptor. Thus, EP1 antagonists may be good candidates as chemopreventive agents for colon **cancer**.

OF 19 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2002179026 MEDLINE

DOCUMENT NUMBER: 21908116 PubMed ID: 11911260

TITLE: Evaluation of a selective prostaglandin E receptor EP1 antagonist for potential properties in colon carcinogenesis.

AUTHOR: Kawamori T; Uchiya N; Kitamura T; Ohuchida S; Yamamoto H; Maruyama T; Sugimura T; Wakabayashi K

CORPORATE SOURCE: Cancer Prevention Division, National Cancer Center Research Institute, Tokyo, Japan.. tkawamor@gan2.ncc.go.jp

SOURCE: ANTICANCER RESEARCH, (2001 Nov-Dec) 21 (6A) 3865-9. Journal code: 8102988. ISSN: 0250-7005.

PUB. COUNTRY: Greece

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200204

ENTRY DATE: Entered STN: 20020326  
Last Updated on STN: 20020420  
Entered Medline: 20020419

AB BACKGROUND: Cyclooxygenases (COXs) and prostanoids play pivotal roles in colon carcinogenesis. This study was designed to determine the chemopreventive effects of ONO-8711, a selective prostaglandin E receptor EP1 antagonist, on the development of azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in male F344 rats and to compare its potential with that of nimesulide, a well-documented selective COX-2 inhibitor. MATERIALS AND METHODS: Five-week-old male F344 rats received s.c. injections of AOM (15 mg/kg body weight) or the saline vehicle once weekly for two weeks and were fed the control diet (AIN-76A) or the experimental diets containing 400 or 800 ppm of ONO-8711 or 400 ppm nimesulide for 5 weeks. RESULTS: Administration of ONO-8711 at 800 ppm significantly reduced the total number of ACF/colon and 5-bromodeoxyuridine (BrdUrd) labeling index as compared to the control diet group (by 31% and 66%, respectively). As expected, dietary administration of nimesulide also suppressed the development of ACF and BrdUrd labeling index in the colon, by about 39% and 54%, respectively. CONCLUSION: Our finding that ONO-8711 significantly suppresses colonic ACF formation and cell proliferation strengthens the hypothesis that the selective **prostaglandin E receptor EP1** antagonists possesses chemopreventive **activity** against colon cancer development.

GenBank  
Entry

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5686498 9/99

RESULT 1  
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LOCUS AC008569 227245 bp DNA linear PRI 05-SEP-2001  
DEFINITION Homo sapiens chromosome 19 clone CTC-548K16, complete sequence.  
ACCESSION AC008569  
VERSION AC008569.7 GI:15431055  
KEYWORDS HTG.  
SOURCE human.  
ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.  
REFERENCE 1 (bases 1 to 227245)  
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.  
TITLE Direct Submission  
JOURNAL Unpublished  
REFERENCE 2 (bases 1 to 227245)  
AUTHORS DOE Joint Genome Institute.  
TITLE Direct Submission  
JOURNAL Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint  
Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA  
REFERENCE 3 (bases 1 to 227245)  
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.  
TITLE Direct Submission  
JOURNAL Submitted (08-NOV-2000) DOE Joint Genome Institute, 2800 Mitchell  
Drive, Walnut Creek, CA 94598, USA  
REFERENCE 4 (bases 1 to 227245)  
AUTHORS DOE Joint Genome Institute and Stanford Human Genome Center.  
TITLE Direct Submission  
JOURNAL Submitted (05-SEP-2001) DOE Joint Genome Institute, 2800 Mitchell  
Drive, Walnut Creek, CA 94598, USA  
COMMENT On Sep 5, 2001 this sequence version replaced gi:11120757.  
Draft Sequence Produced by DOE Joint Genome Institute  
www.jgi.doe.gov  
Finishing Completed at Stanford Human Genome Center  
www-shgc.stanford.edu  
Quality: Phrap Quality >=40 99.8% of Sequence;  
Estimated Total Number of Errors is 0.3.  
STS Content:  
SHGC-23895 G28498  
SHGC-141627 G63606  
SHGC-35463 G29823  
SHGC-31833 G29335.  
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BASE COUNT 54928 a 59916 c 58482 g 53919 t  
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Best Local Similarity 99.9%; Pred. No. 0;  
Matches 3906; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

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Qy 3901 tttgggaa 3908
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Db 207100 TTTGGGAA 207093

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RESULT 4

HUMG

LOCUS HUMG 1376 bp mRNA linear PRI 03-JAN-1994

DEFINITION Human prostaglandin receptor epl subtype mRNA, complete cds.

ACCESSION L22647

VERSION L22647.1 GI:410208

KEYWORDS prostaglandin receptor epl subtype.

SOURCE Homo sapiens cDNA to mRNA.

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 1376)

AUTHORS Funk,C.D., Furci,L., FitzGerald,G.A., Grygorczyk,R., Rochette,C., Bayne,M.A., Abramovitz,M., Adam,M. and Metters,K.M.

TITLE Cloning and expression of a cDNA for the human prostaglandin E receptor EP1 subtype

JOURNAL J. Biol. Chem. 268 (35), 26767-26772 (1993)

MEDLINE 94075377

REFERENCE 2 (bases 1 to 1376)

AUTHORS Funk,C.D.

TITLE Direct Submission

JOURNAL Submitted (01-NOV-1993) Colin D. Funk, Department of Pharmacology, Vanderbilt University, Nashville, TN 37232, USA

FEATURES

Location/Qualifiers

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CDS 75. .1283

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3'UTR 1284. .1376

polyA\_signal 1358. .1363

BASE COUNT 138 a 526 c 484 g 228 t

ORIGIN

Query Match 24.7%; Score 967; DB 9; Length 1376;

Best Local Similarity 97.0%; Pred. No. 9.8e-101;

Matches 985; Conservative 0; Mismatches 30; Indels 0; Gaps 0;

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LOCUS AR086516 1394 bp DNA linear PAT 07-SEP-2000

DEFINITION Sequence 3 from patent US 5985597.

ACCESSION AR086516

VERSION AR086516.1 GI:10013282

KEYWORDS .

SOURCE Unknown.

ORGANISM Unknown.

Unclassified.

REFERENCE 1 (bases 1 to 1394)

AUTHORS Ford-Hutchinson,A., Funk,C., Grygorczyk,R. and Metters,K.

TITLE DNA encoding prostaglandin receptor EP1

JOURNAL Patent: US 5985597-A 3 16-NOV-1999;

FEATURES Location/Qualifiers

source 1. .1394

/organism="unknown"

BASE COUNT 157 a 525 c 484 g 228 t

ORIGIN

Query Match 24.7%; Score 967; DB 6; Length 1394;  
 Best Local Similarity 97.0%; Pred. No. 9.7e-101;  
 Matches 985; Conservative 0; Mismatches 30; Indels 0; Gaps 0;

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LOCUS AX280933 1209 bp DNA linear PAT 02-NOV-2001

DEFINITION Sequence 556 from Patent WO0177172.

ACCESSION AX280933

VERSION AX280933.1 GI:16608222

KEYWORDS .

SOURCE human.

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (sites)

AUTHORS Lehmann-Bruinsma, K., Liaw, C.W. and Lin, I.L.

TITLE Non-endogenous, constitutively activated known G protein-coupled receptors

JOURNAL Patent: WO 0177172-A 556 18-OCT-2001;

Arena Pharmaceuticals, Inc. (US)

FEATURES Location/Qualifiers

source 1..1209

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BASE COUNT 107 a 469 c 424 g 209 t

ORIGIN

Query Match 24.1%; Score 944.4; DB 6; Length 1209;

Best Local Similarity 96.9%; Pred. No. 3.6e-98;

Matches 963; Conservative 0; Mismatches 31; Indels 0; Gaps 0;

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